(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
21 May 2004 (21.05.2004)

PCT

(10) International Publication Number
WO 2004/041851 A3

(51) International Patent Classification[7]: C07K 14/16, A61K 39/21, C12N 15/48, A61K 48/00, C12N 15/62

(21) International Application Number: PCT/EP2003/012429

(22) International Filing Date: 3 November 2003 (03.11.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0225786.3 5 November 2002 (05.11.2002) GB

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(72) Inventor; and

(75) Inventor/Applicant *(for US only)*: **ERTL, Peter, Franz** [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY (GB).

(74) Agent: **PRIVETT, Kathryn, Louise**; GlaxoSmithKline (CN925.1), 980 Great West Road, Brentford, Middlesex TW8 9GS (GB).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

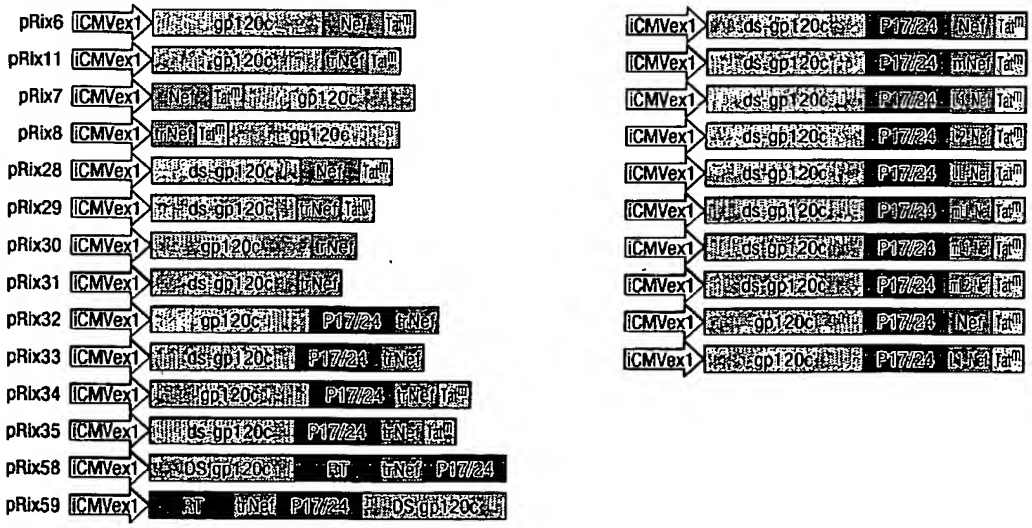
Published:
— *with international search report*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

(88) Date of publication of the international search report: 17 March 2005

[Continued on next page]

(54) Title: VACCINE

A Schematic representation of further constructs



(57) Abstract: The invention relates to polynucleotides for DNA vaccination which polynucleotides encode an HIV envelope protein or fragment or immunogenic derivative fused to an additional HIV protein selected from a non-structural protein or capsid protein or fragment or immunogenic derivative thereof. Preferably the HIV envelope molecule is gp120 and preferred fusions include one or more of HIV Nef, Gag, RT or Tat. Preferably the HIV envelope molecule is non-glycosylated in mammalian cells.

WO 2004/041851 A3

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 03/12429

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07K14/16 A61K39/21 C12N15/48 A61K48/00 C12N15/62

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE, MEDLINE, CHEM ABS Data, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WOODBERRY T ET AL: "Immunogenicity of a human immunodeficiency virus (HIV) polytope vacine containing multiple HLA A2 HIV CD8+ cytotoxic T-cell epitopes" JOURNAL OF VIROLOGY, THE AMERICAN SOCIETY FOR MICROBIOLOGY, US, vol. 73, no. 7, July 1999 (1999-07), pages 5320-5325, XP002162348 ISSN: 0022-538X	1-6, 10-12, 17-31
Y	the whole document	13-16
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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
31 August 2004	11. 01. 05

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Morawetz, R

Form PCT/ISA/210 (second sheet) (January 2004)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 03/12429

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LIU W J ET AL: "Papillomavirus Virus-like Particles for the Delivery of Multiple Cytotoxic T Cell Epitopes" VIROLOGY, ACADEMIC PRESS,ORLANDO, US, vol. 273, no. 2, 1 August 2000 (2000-08-01), pages 374-382, XP004436241 ISSN: 0042-6822	1-3,6, 11,12, 17-21, 23-31
Y	the whole document	4,5, 13-16,22
X	WO 01/27291 A (LANGLADE DEMOYEN PIERRE ;FIRAT HUESEYIN (FR); LEMONNIER FRANCOIS () 19 April 2001 (2001-04-19)	1-6, 10-12, 17-31
Y	figure 5; example 11; tables 5-8	13-16
X	WO 02/32943 A (CHADRABARTI BIMAL K ;HUANG YUE (US); US GOVERNMENT (US); NABEL GAR) 25 April 2002 (2002-04-25)	1-3,6, 11,13, 14, 17-21, 23-31
Y	the whole document	4,5,12, 15,16,22
X	EP 0 577 894 A (GREEN CROSS KOREA) 12 January 1994 (1994-01-12)	1-3, 10-12, 17-21, 23-31
Y	the whole document	4,5,13, 15,16,22
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INTERNATIONAL SEARCH REPORT

International Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	DOE B ET AL: "INDUCTION OF HIV-1 ENVELOPE (GP120)-SPECIFIC CYTOTOXIC T LYMPHOCYTE RESPONSES IN MICE BY RECOMBINANT CHO CELL-DERIVED GP120 IS ENHANCED BY ENZYMATIC REMOVEL OF N-LINKED GLYCANS" EUROPEAN JOURNAL OF IMMUNOLOGY, WEINHEIM, DE, vol. 24, no. 10, 1994, pages 2369-2376, XP000672290 ISSN: 0014-2980 the whole document	11
Y	BOTARELLI P ET AL: "N-GLYCOSYLATION OF HIV-GP120 MAY CONSTRAIN RECOGNITION BY T LYMPHOCYTES" JOURNAL OF IMMUNOLOGY, THE WILLIAMS AND WILKINS CO. BALTIMORE, US, vol. 147, no. 9, 1 November 1991 (1991-11-01), pages 3128-3132, XP000673664 ISSN: 0022-1767 the whole document	11,12,14
Y	STEFANIE A ET AL: "Increased Immune Response Elicited by DNA Vaccination with a Synthetic gp120 Sequence with Optimized Codon Usage" JOURNAL OF VIROLOGY, THE AMERICAN SOCIETY FOR MICROBIOLOGY, US, vol. 72, no. 2, February 1998 (1998-02), pages 1497-1503, XP002278034 ISSN: 0022-538X the whole document	13,14
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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 03/12429

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	IGLESIAS, ENRIQUE ET AL: "Chimeric proteins containing HIV-1 T cell epitopes: Expression in E. coli, purification and induction of antibodies in mice" JOURNAL OF BIOCHEMISTRY, MOLECULAR BIOLOGY AND BIOPHYSICS , 5(2), 109-122 CODEN: JBMBF6; ISSN: 1025-8140, 2001, XP009035847 the whole document	1-6, 10-31
X	CA 2 430 702 A (CT DE INGENIERIA GENETICA Y BI) 6 September 2002 (2002-09-06) the whole document	1-6, 10-31
E	WO 2004/041852 A (GLAXO GROUP LTD ; ERTL PETER FRANZ (GB)) 21 May 2004 (2004-05-21) the whole document	1-6, 10-31

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 03/12429

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claim 28 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [X] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

1-6,10-31

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[X] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 6 (completely) 1-3, 10-21, 23-31 (all partially)

A polynucleotide which comprises a sequence encoding an HIV envelope protein or fragment or immunogenic derivative thereof, fused to at least one sequence encoding an HIV non-structural or capsid protein or fragment or immunogenic derivative thereof, operably linked to a hetereologous promoter.

1.1. claims: 6 (completely) 1-3, 11-21, 23-31 (all partially)

A polynucleotide which comprises a sequence encoding an HIV envelope protein or fragment or immunogenic derivative thereof, fused to at least one sequence encoding an HIV non-structural or capsid protein or fragment or immunogenic derivative thereof, operably linked to a hetereologous promoter, wherein the at least one structural or capsid protein or fragment or immunogenic derivative thereof is selected from Nef, and subject-matter related thereto.

1.2. claims: 1-3, 10-13, 15-21, 23-31 (all partially)

A polynucleotide which comprises a sequence encoding an HIV envelope protein or fragment or immunogenic derivative thereof, fused to at least one sequence encoding an HIV non-structural or capsid protein or fragment or immunogenic derivative thereof, operably linked to a hetereologous promoter, wherein the at least one structural or capsid protein or fragment or immunogenic derivative thereof is selected from Gag, and subject-matter related thereto.

1.3. claims: 1-3, 11-13, 15-21, 23-31 (all partially)

A polynucleotide which comprises a sequence encoding an HIV envelope protein or fragment or immunogenic derivative thereof, fused to at least one sequence encoding an HIV non-structural or capsid protein or fragment or immunogenic derivative thereof, operably linked to a hetereologous promoter, wherein the at least one structural or capsid protein or fragment or immunogenic derivative thereof is selected from RT, and subject-matter related thereto.

1.4. claims: 1-3, 11-13, 15-21, 23-31 (all partially)

A polynucleotide which comprises a sequence encoding an HIV envelope protein or fragment or immunogenic derivative thereof, fused to at least one sequence encoding an HIV non-structural or capsid protein or fragment or immunogenic derivative thereof, operably linked to a hetereologous promoter, wherein the at least one structural or capsid protein or fragment or immunogenic derivative thereof is selected from Tat, and subject-matter related thereto.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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2. claims: 4, 5, 22 (all completely), 1-3, 10-21, 23-31 (all partially)

A polynucleotide which comprises a sequence encoding an HIV envelope protein or fragment or immunogenic derivative thereof, fused to at least one sequence encoding an HIV non-structural or capsid protein or fragment or immunogenic derivative thereof, operably linked to a hetereologous promoter, wherein the polynucleotide encodes a gp120, RT, Gag and Nef-containing fusion protein, and subject-matter related thereto.

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3. claims: 7,8 (all completely), 1-3, 11-21, 23-31 (all partially)

A polynucleotide which comprises a sequence encoding an HIV envelope protein or fragment or immunogenic derivative thereof, fused to at least one sequence encoding an HIV non-structural or capsid protein or fragment or immunogenic derivative thereof, operably linked to a hetereologous promoter, wherein the polynucleotide encodes a gp120, Tat and Nef-containing fusion protein, and subject-matter related thereto.

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4. claims: 9 and 32-34 (all completely), 1-3, 10-21, 23-31 (all partially)

A polynucleotide which comprises a sequence encoding an HIV envelope protein or fragment or immunogenic derivative thereof, fused to at least one sequence encoding an HIV non-structural or capsid protein or fragment or immunogenic derivative thereof, operably linked to a hetereologous promoter, wherein the polynucleotide encodes a gp120-Gag-Nef-Tat fusion, and subject-matter related thereto. A polynucleotide encoding an HIV Tat molecule or fragment or immunogenic derivative in a fusion with at least two further HIV antigens, and subject-matter related thereto.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/EP 03/12429

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533,841

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
21 May 2004 (21.05.2004)

PCT

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(51) International Patent Classification[7]: C07K 14/005

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(71) Applicant *(for all designated States except US)*: **GLAXO GROUP LIMITED** [GB/GB]; Glaxo Wellcome House, Berkeley Avenue, Greenford, Middlesex UB6 0NN (GB).

(72) Inventor; and

(75) Inventor/Applicant *(for US only)*: **ERTL, Peter, Franz** [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY (GB).

(74) Agent: **PRIVETT, Kathryn, Louise**; GlaxoSmithKline (CN925.1), 980 Great West Road, Brentford, Middlesex TW8 9GS (GB).

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(84) Designated States *(regional)*: ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *without international search report and to be republished upon receipt of that report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: VACCINE

(57) Abstract: The invention relates to polynucleotides for DNA vaccination which polynucleotides encode an HIV envelope protein or fragment or immunogenic derivative fused to an additional HIV protein selected from a non-structural protein or capsid protein or fragment or immunogenic derivative thereof. Preferably the HIV envelope molecule is gp120 and preferred fusions include one or more of HIV Nef, Gag, RT or Tat. Preferably the HIV envelope molecule is non-glycosylated in mammalian cells.

WO 2004/041851 A2